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1: Proc Natl Acad Sci U S A. 1997 Jun 24;94(13):6916-21.

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Efficient photoreceptor-targeted gene expression in vivo by recombinant adeno-associated virus.

Flannery JG, Zolotukhin S, Vaquero MI, LaVail MM, Muzyczka N, Hauswirth WW.

School of Optometry and Neuroscience Group, University of California, Berkeley, CA 94720, USA.

We describe a general approach for achieving efficient and cell type-specific expression of exogenous genes in photoreceptor cells of the mammalian retina. Recombinant adeno-associated virus (rAAV) vectors were used to transfer the bacterial lacZ gene or a synthetic green fluorescent protein gene (gfp) to mouse or rat retinas after injection into the subretinal space. Using a proximal murine rod opsin promoter (+86 to -385) to drive expression, reporter gene product was found exclusively in photoreceptors, not in any other retinal cell type or in the adjacent retinal pigment epithelium. GFP-expressing photoreceptors typically encompassed 10-20% of the total retinal area after a single 2-microl injection. Photoreceptors were transduced with nearly 100% efficiency in the region directly surrounding the injection site. We estimate approximately 2.5 million photoreceptors were transduced as a result of the single subretinal inoculation. This level of gene transfer and expression suggests the feasibility of genetic therapy for retinal disease. The gfp-containing rAAV stock was substantially free of both adenovirus and wild-type AAV, as judged by plaque assay and infectious center assay, respectively. Thus, highly purified, helper virus-free rAAV vectors can achieve high-frequency tissue-specific transduction of terminally differentiated, postmitotic photoreceptor cells.

PMID: 9192666 [PubMed - indexed for MEDLINE]

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